Long-term Evaluation of Peri-implant Bone Level after Reconstruction of Severely Atrophic Edentulous Maxilla via Vertical and Horizontal Guided Bone Regeneration in Combination with Sinus Augmentation: A Case Series with 1 to 15 Years of Loading

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ABSTRACT

Background: To the best of the authors' knowledge, there is very limited clinical data on the outcomes of simultaneous guided bone regeneration (GBR) for horizontal and/or vertical bone gain for the reconstruction of severely atrophic edentulous maxilla. Therefore, the purpose of the clinical series presented herein was to clinically evaluate long-term horizontal and vertical bone gain, as well as implant survival rate after reconstruction of severely atrophic edentulous maxillary ridges.

Material and Methods: Sixteen patients (mean age: 64.6 ± 14.6 years of age) were consecutively treated for vertical and/or horizontal bone augmentation via GBR in combination with bilateral sinus augmentation utilizing a mixture of autologous and anorganic bovine bone. Implant survival, bone gain, intraoperative/postoperative complications and peri-implant bone loss were calculated up to the last follow-up exam.

Results: Overall, 122 dental implants were placed into augmented sites and have been followed from 12 to 180 months (mean: 76.5 months). Implant survival was 100% (satisfactory survival rate of 97.5%). Mean bone gain was 5.6 mm (max: 9 mm; min: 3 mm) While vertical bone gain was 5.1 ± 1.8 mm; horizontal bone gain was 7.0 ± 1.5 mm. No intraoperative/postoperative complications were noted. Mean peri-implant bone loss values were consistent within the standards for implant success (1.4 ± 1.0 mm). At patient-level, only one patient who had three implants presented with severe peri-implant bone loss.

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Disclaimers: Dr. Urban and Dr. Wang received honoraria for lecturing from Osteogenics Biomedical. In addition, Dr. Urban received honoraria for lecturing from Geistlich Pharma AG and from Nobel Biocare AB.

One Sentence Summary: Complete maxillary reconstruction can be successfully achieved via GBR and sinus augmentation.

DOI 10.1111/cid.12431

Conclusion: Complete reconstruction of an atrophied maxilla can be successfully achieved by means of guided bone regeneration for horizontal and/or vertical bone gain including bilateral sinus augmentation using a mixture of anorganic bovine bone and autologous bone.

KEY WORDS: edentulous maxilla, guided bone regeneration, horizontal ridge augmentation, maxillary reconstruction, sinus augmentation, vertical ridge augmentation

INTRODUCTION

Bone remodeling after tooth extraction often leads to inadequate ridge dimensions for ideal three-dimensional implant position.[1,2] Bone augmentation, horizontal and/or vertical, is often the procedure performed to overcome these deficiencies.[3] Block grafting has been advocated for the correction of larger bone deficiencies.[4–6] Nonetheless, the increased morbidity of recipient site or long-term volumetric instability has encouraged clinicians to utilize alternatives.[7–9] In the posterior maxilla, besides the bone resorption, the proximity of the maxillary sinus often results in inadequate bone for implant placement. The use of short or tilted implants has also been proposed to avoid major bone augmentation procedures.[10–12] Nevertheless, these alternative approaches lack long-term studies to support their long-term effectiveness. On the other hand, sinus augmentation via the lateral wall approach was developed to overcome severe vertical bone deficiency in the maxillary posterior region. And its predictability and safety have been demonstrated since 1980 by means of bone formation, low complication rates, and high implant success rates,[13–15] regardless of the residual crestal bone height.[16]

For minor and moderate ridge defects, guided bone regeneration (GBR) offers the possibility of restoring the reabsorbed bone architecture through the application of particulated bone graft materials in conjunction with barrier membranes to stabilize and protect the graft materials placed.[17] Recently, GBR using resorbable membranes has been shown to correct/augment "knife edge" ridges.[18–20] Nonetheless, when intended to augment vertically, titanium reinforced d-PTFE membranes may present a better choice due to their ability to maintain/create space that is necessary for bone augmentation.[21–27] PASS principle (primary wound closure, angiogenesis, space and stability of the clot) remains a corner stone for successful GBR.[28] A combination of ridge and sinus augmentation for partially edentulous patients has been documented with high medium-term implant survival.[16,22,24,25]

In the arena of GBR as well as sinus augmentation, a wide variety of materials have been investigated.[14,15] So far, no consensus has been reached with regards to the clinical superiority.[15] Two of the most commonly reported biomaterials, autologous bone (AB) and anorganic bovine bone mineral (ABBM), have shown equal implant survival rates between the two as well as similar results compared to implants placed in pristine bone.[29,30] However, their histological characteristics differ significantly.[31–33] While the sole use of ABBM provides good space maintenance, less vital bone formation may be expected due to the slow turnover that leads to the higher proportion of remaining material.[34] On the other hand, it has been demonstrated that the use of ABBM provides significantly higher bone gain if mixed with at least 40% of AB.[35] This histologic enhancement is due to the osteogenic potential of AB. However, the use of AB solely is discouraged, particularly for large defects, due to the potential resorption.[36,37]

Since there is very limited clinical data on the outcomes of simultaneous guided bone regeneration (GBR) for horizontal and/or vertical bone gain for the reconstruction of the severely atrophic edentulous maxilla, the clinical series reported herein was aimed at evaluating bone gain over these procedures longitudinally as well as the related implant survival rate.

MATERIAL AND METHODS

Subject Recruitment

From September 1999 through April 2013, 16 patients presented with knife-edge ridges that had insufficient width (<6 mm)[38] and height (<10 mm)[11] and these patients were recruited and consecutively treated in this case series. All patients (mean age: 64.68 ± 14.68 years of age) required horizontal ($N = 7$), vertical ($N = 6$), or both ($N = 3$) hard tissue reconstructions

TABLE 1 Clinical and Radiographic Characteristics of the Subjects Included in the Present Study

Patient	Age (years)	Type of Defect	Defect (Baseline – mm)	Grafted Area (8 months – mm)	Complications	No Implants	Mean MBL	Mena Follow-up (months)
1	80	Vertical	2	10	No	7	1.3	180
2	69	Vertical	2	10	No	8	2.7	144
3	68	Horizontal	1	9	No	8	0.4	120
4	70	Horizontal	3	9	No	8	1.7	120
5	73	Vertical	5	10	No	5	3.6	120
6	62	Vertical	6	10	No	9	1.0	108
11	66	Horizontal	2.5	8	No	7	1.1	96
7	67	Horizontal	2	11	No	8	2.1	72
8	72	Horizontal	1	9	No	8	0.5	60
9	67	Vertical	5	10	No	8	2.0	48
10	66	Vertical	9	13	No	6	0.3	48
12	48	Vertical	2	7	No	9	1.0	36
13	50	Vertical	2	5	No	8	1.7	24
14	58	Vertical/Horizontal	6	10	No	8	0.5	24
15	60	Horizontal	2	8	No	7	1.7	12
16	59	Horizontal	2	10	No	8	0.3	12
Overall	64.68		3.71	9.31	No (100%)	122	1.4	76.56

to augment Cawood-Howell class IV-VI (Table 1) resorbed maxillary ridges for subsequent implant placement, including bilateral sinus augmentation. All patients were treated in a private practice (Budapest, Hungary), and all surgical procedures were performed by the same practitioner (I. U.) with over 20 years of experience in oral surgery and implant therapies. The prosthetic treatments were performed and restored by the author (I. U.) and other private practitioners. All patients included in the case series were in good physical health, able to maintain good oral hygiene, and were treated with a GBR membrane and bone graft. Patients were not eligible for this treatment if they were current smokers, engaged in excessive alcohol consumption, or had uncontrolled systemic conditions or uncontrolled periodontal disease.

Clinical Procedure

Patients were treated with ridge augmentation using either a dense titanium reinforced non-resorbable membrane (d-PTFE; Cytoplast™ Ti-250 Titanium-Reinforced Membrane, Osteogenics Biomedical, Inc., Lubbock, Texas – 4 cases), a titanium reinforced expanded polytetrafluoroethylene non-resorbable membrane (e-PTFE; GORE-TEX® Regenerative Membrane, Titanium-Reinforced; W.L. Gore & Associates, Flagstaff, AZ – 4 cases), or an resorbable membrane (GORE RESOLUT® ADAPT® LT Regenerative Membrane, W.L. Gore & Associates, Inc., Flagstaff, AZ – 3 cases) or (Bio-Gide® Resorbable Bilayer Membrane, Geistlich Pharma AG, Wolhusen, Switzerland – 9 cases). Autogenous particulated bone or a 1:1 ratio of autogenous bone and anorganic bovine bone-derived mineral (ABBM, Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland) were used as the bone graft for all treatments. The surgical site was left to heal for an average of 8 months to allow bone maturation. After the bone healing period, 122 implants were placed (114 anodized TiUnite and 8 acid etched Steri-Oss implants, Nobel Biocare, Gothenburg, Sweden). The selection of implants for each patient was not random but was based on the quality/quantity of bone at the respective implant sites.

Pre-surgical Procedure

Patients were premedicated with amoxicillin 2 g 1 hour before surgery and 500 mg penicillin three times a day for one week following the surgery. In the event of a penicillin allergy, clindamycin 600 mg was used for premedication and 300 mg four times a day for one week following surgery. Oral sedation, usually Triazolam 0.50 mg, was also frequently administered

one-hour prior to surgery. Patients were instructed to rinse with 0.2% chlorhexidine solution for one minute to disinfect the surgical site and a sterile surgical drape was applied to minimize the potential contamination from extraoral sources. Surgery area was numbed using a local anesthetic agent with adrenaline 1/100,000. In eight patients general anesthesia was utilized.

Guided Bone Augmentation for Horizontal and/or Vertical Reconstruction

As described previously,[19,20,27] the flap design was aimed at primary tension-free closure after the bone grafting procedure despite the increased dimension of the ridge. A remote flap was performed including crestal and vertical releasing incisions. A full thickness, mid-crestal incision into the keratinized mucosa was performed with a surgical scalpel (Number 15). The two divergent vertical incisions were placed at least one tooth away from the surgical site. In edentulous areas, the vertical incisions were placed at least 5 mm away from the augmentation site. After primary incisions, periosteal elevators were used to reflect a full thickness flap beyond the mucogingival junction and at least 5 mm beyond the bone defect. After flap elevation and evaluation of the defect size, autogenous bone was harvested from the retromolar regions in eleven patients using a trephine bur. In four patients the chin was used for bone harvest and in one patient the bone was harvested from the hip. The harvested graft was particulated in a bone mill (R. Quétin Bone-Mill, Roswitha Quétin Dental Products, Leimen, Germany) and then either applied alone or after preparing a 1:1 mixture with ABBM (the combination is referred to as "composite bone graft"). The bone of the exposed augmentation site was cleaned of all soft tissue remnants prior to grafting. Ridge measurements were taken and are described in a section below. The recipient bone bed was prepared with multiple decorticalization holes using a small round bur. The membrane was fixed to at least two points on the lingual/palatal sides with titanium pins. The autogenous particulated bone graft or composite bone graft was placed into the defect, and the membrane was folded over and fixed in place with additional titanium pins on the vestibular side.

Sinus Augmentation Procedure

The surgical technique for the lateral window approach has been described previously.[16] Briefly, a full thickness periosteal flap was elevated to expose the lateral wall of the sinus. After the sinus window was prepared and infractured, the Schneiderian membrane was lifted carefully to allow for placement of implants 13 to 15 mm in length.

In all procedures, a sagittal sandwich layer bone graft was created with ABBM and the harvested, particulated AB. ABBM was applied and packed to the medial wall of the sinus. The autogenous bone was then applied and packed exactly superior to the planned implant sites on the ridge. Then, the autogenous bone layer was covered laterally with a final layer of ABBM. An resorbable collagen membrane was applied to the area to protect the sinus windows.

Membrane Placement

An appropriately sized membrane was selected and trimmed so that it covered the volume of the graft. In most cases several membranes had to utilized to cover the entire graft. In cases when horizontal ridge augmentation was performed, a resorbable membrane was utilized. In vertical and combined horizontal and vertical bone augmentation cases a non-resorbable, titanium reinforced membrane was selected. Membranes' selection was based on commercial availability.

The membranes were stabilized first on the palatal sides using titanium pins or short, 3 mm titanium screws on at least two points. The autogenous particulated bone graft was placed on the defect and then the membrane was folded over and stabilized with additional titanium pins or screws carefully as the facial bone wall was often very thin and fragile.

Soft Tissue Management

Once the membrane was completely secured, the flap was mobilized to permit tension free, primary closure. A periosteal releasing incision connecting the two vertical incisions was performed to achieve elasticity of the flap. The flap was than sutured in two layers: first horizontal mattress sutures (GORE-TEX® CV-5 Suture, W.L. Gore & Associates, Inc., Flagstaff, AZ, or Cytoplast 3-0 Suture, Osteogenics Biomedical, Inc., Lubbock, Tx, USA) were placed 4 mm from the incision line; then, single interrupted sutures with the same PTFE suture were placed to close the edges of

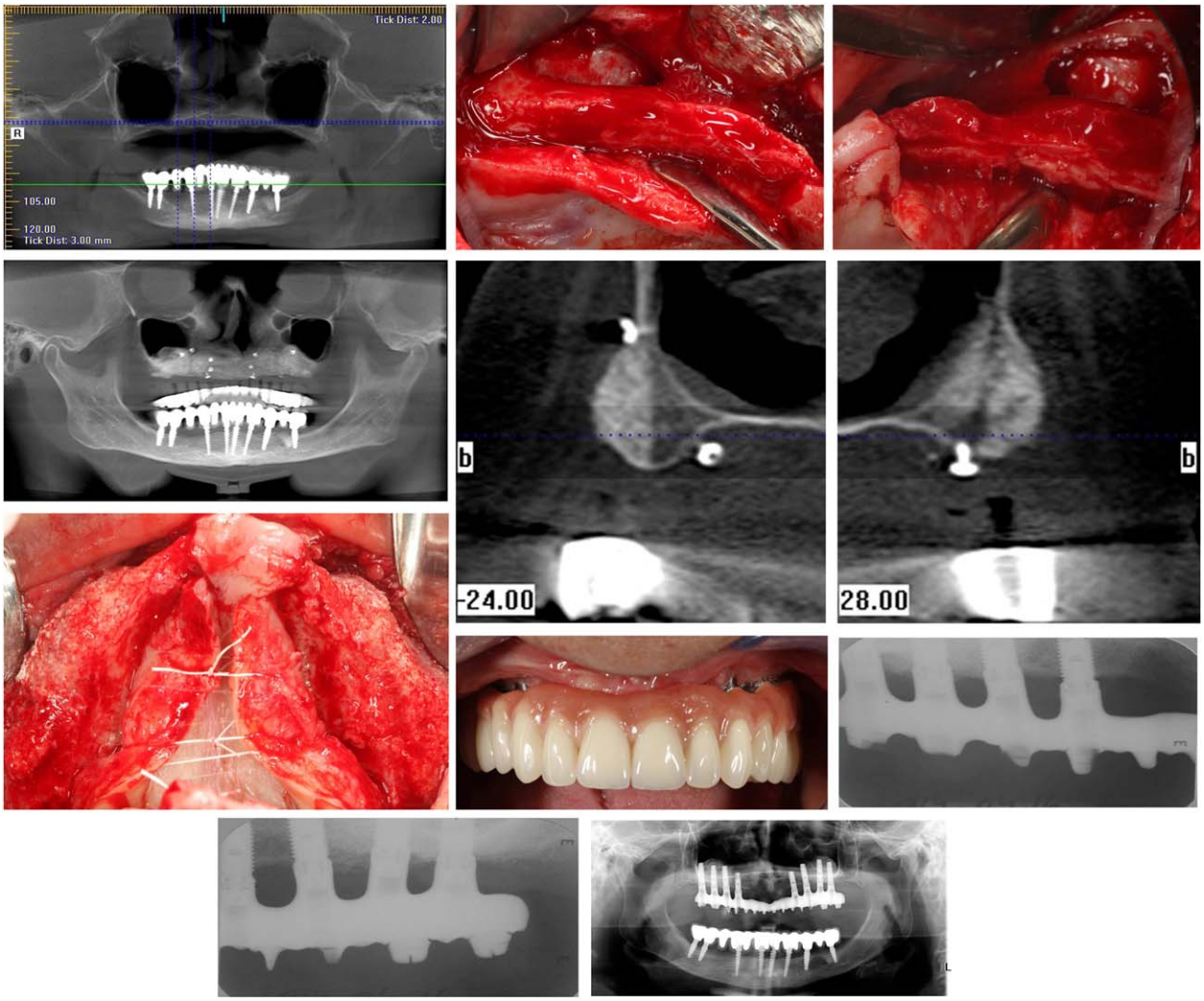

Figure 1 Five-year follow-up of a 60-year old female after reconstruction of an edentulous and severely resorbed maxilla. (**1**) Panoramic view of a severely resorbed maxillary case. (**2** and **3**) Occlusal views of the ridge atrophies. (**4** to **6**) Panoramic and cross sectional views of the reconstructed ridge. (**7**) Occlusal view of the regenerated maxilla. (**8**) Labial view of the final fixed implant supported maxillary complete denture (bridge). (**9** and **10**) Periapical radiographs after 5 years of loading. (**11**) Panoramic radiograph of the reconstruction. Note that the lower jaw was reconstructed before the patient sought treatment from the author.

the flap, leaving at least a 4 mm thick connective tissue layer between the membrane and the oral epithelium. This intimate connective tissue-to-connective tissue contact provides a barrier preventing exposure of the membrane. Vertical incisions were closed with single interrupting sutures. The single interrupted sutures were removed between 10 to 14 days post surgery, and mattress sutures were removed after two to three weeks.

Bone Gain and Complications

Measurements of the alveolar ridge width were taken at the time of grafting and then at implant placement. The same caliper was used to take all measurements 2 mm apically from the top of the crest. Periapical x-rays were taken at the abutment connection and every year thereafter with a long cone paralleling technique. Complications in bone graft healing, such as membrane exposure, subsequent infection, and/ or morbidity associated with the harvest site, were recorded. Functionally loaded implants were monitored to evaluate the following: absence of pain, foreign body sensation, dyesthesia; radiological contact between the host and rated according to the Consensus of Pisa statement on implant survival, success and failure.[39]

Radiographic Peri-implant Bone Level

Implant bone level was determined by periapical radiographs using the ImageJ64 (http://rsb.info.nih.gov/ij/

docs/install/osx.html). To determine marginal bone loss (MBL), one independent calibrated examiner made linear measurements on each implant in every periapical radiograph from the most mesial and distal point of the implant platform or the rough/smooth surface interface (depending on the implant macro-design) to the crestal bone level at the longest follow-up radiographic evaluation. Cohen's kappa intra- and interexaminer coefficients were used to test reliability.

RESULTS

Horizontal and or Vertical Bone Gain and Complications

Healing of the bone graft was uneventful in all 16 patients and all sites achieved adequate horizontal and vertical bone dimensions after undergoing the combination of grafting procedures with sinus augmentation. Mean bone gain was 5.6 mm (max: 9 mm; min: 3 mm) with vertical bone gain of 5.1 ± 1.8 mm and horizontal bone gain of 7.0 ± 1.5 mm. For sites where horizontal and vertical bone augmentations were attempted, only vertical bone gain was reported. The amount of vertical bone gain was positively associated with defect atrophy. In other words, the more severe the defect was, the more vertical bone gain was achieved (Figure 1).

Implant Survival

All 122 implants (114 Brånemark Mk III, IV, NobelSpeedy, and NobelReplace; and 8 Steri-Oss) could be placed according to their predetermined optimal prosthetic positions and assessed on their longest follow-up radiographic examination (mean follow-up: 76.5 months) Implant survival rate was 100%.[40] According to the Pisa Consensus Conference standards,[39] a satisfactory survival rate of 97.6% was reported for this case series, as defined by (1) no pain on function, (2) 0 mobility, (3) 2–4 mm radiographic bone loss, and (4) no exudate history. Only 2.4% were shown to have compromised survival due to radiographic bone loss >4 mm, although none of the other items listed for this category were found.

Peri-implant Bone Level

Cohen's kappa intra-examiner coefficient was used to test reliability of the measurements. This analysis indicated a high degree of accuracy in the measurements. An overall, 244 interimplant bone levels were available to be measured at baseline (implants' healing abutment placement), and up to the latest long-term examination (mean: 76.5 months). Mean peri-implant bone loss values were consistent within the standards for success in implant dentistry (1.4 ± 1 mm). MBL was found to increase over time (1 mm, 1.7 mm, and 2.0 mm, for ≤ 60 month, 60–120 month and >120 month assessment, respectively. At patient-level, only one patient followed for 120 months had three implants with severe peri-implant bone loss (>5 mm – 2.4% from the overall sample) but less than half of implant body. When assessing the frequency distribution of MBL, it was found that 31.9%, 43.4%, 22.1%, and 2.4% of the implants lost <1 mm, 1–2mm, 2–3mm and >3 mm radiographic bone, respectively.

DISCUSSION

Although sinus augmentation and guided bone augmentation (GBR) for horizontal and vertical bone gain have been shown to be predictable in many reports,[14,16,18–20,22,23,25–27,29,33] little is known about the long-term stability of completely edentulous atrophied ridges by means of peri-implant stability and bone gain maintenance. The present case series demonstrated that with proper soft and hard tissue management, bone gain can be predictably maintained over time. The current result is in agreement with previous studies[41–43] as well as systematic reviews,[30,44] illustrating implant survival rate and peri-implant bone level in the grafted bone are comparable to implants placed in native bone. Similarly, it occurs for implants placed in augmented sinuses;[14] nonetheless, controversy exists regarding peri-implant bone stability.[45,46] Moreover, Jung et al.[43] showed the long-term effectiveness and stability of GBR when resorbable and non-resorbable membranes were used in combination with ABBM and AB. The present study highlights the characteristics of this approach for its use in GBR for reconstructive of extensive atrophic ridges. Good implant success rates were reported after vertical GBR using autogenous particulated bone.[22,25,47] In the majority of the patients in this case series, autograft mixed with ABBM was utilized. It has been reported that this combination not only triggers osteoblasts and growth factor release from AB but also maintains a space via ABBM due to its slow

resorption rate.[48,49] This mixture ratio (1:1) may also play an important role on cell migration and proliferation. As stated previously, while ABBM resorbs slowly, AB turns over allowing a favorable invasion of osteoblasts through the creation of a newly formed Haversian system.[50] Therefore, based on clinical, radiographic and histologic evaluation, it seems that this bone grafting mixture is a safe and predictable way to achieve bone gain in the augmented maxillary sinus and for horizontal and/or vertical bone regeneration.

Numerous alternatives have been proposed to overcome bone atrophy in the posterior maxilla in the attempt to reduce the potential complications that might occur in performing above advanced bone-grafting procedures.[10,11,51–54] Nonetheless, sinus augmentation, regardless the bone graft used[55] remains to be the "gold standard" for oral rehabilitation of the severe resorbed maxilla since it allows implant placement in a proper position so a more favorable occlusal force load can be achieved.[56] This technique via the lateral window approach is a well documented, frequently performed, and predictable procedure with established methods. However, this surgical procedure is subjected to potential intraoperative and postoperative complications primarily associated with the maxillary sinus anatomy.[57] It is generally agreed that sinus membrane perforation (19.8%) remains the most common complication during sinus augmentation,[58] which may range from 7–30%[16,59–61] and may potentially lead to infection.[61] In the present study no complications (i.e., membrane perforation or infection) related to sinus augmentation procedures were reported. This may be due to the low sample size (32 sinus augmentation procedures) included in the present study and the expertise of the operator (IU). Thus, these findings must be interpreted cautiously, since the lack of control on clinical parameters regarding sinus anatomy in the present trial may potentially bias our outcome.

Likewise, for GBR, a broad variety of resorbable and nonresorbable have been proven to be effective in excluding fibroblast-like cells ingrowth into the grafted defect.[25,29,43,62] The reinforcement of the membrane with titanium strips makes it more moldable and stable for vertical bone augmentation, especially in large-size defects.[27] Hence it can better maintain the space that is needed for bone ingrowth. However, the main complication of this membrane is exposure, which may significantly jeopardize the final augmentation outcome.[63] Machtei reported in a meta-analysis that sites with membrane exposure had sixfold less bone gain when compared to the sites without exposure (3.0 mm vs. 0.5 mm).[64] A wide range of complication rates have been reported in the literature for this approach (0–45%),[65] however the local cofounding factors (i.e., location, morphology or biomaterials) that influence the outcome remain to be determined. In this regard, soft tissue management then become essential since it is the way to achieve primary wound closure and fulfill the PASS principle for successful GBR.[28] We have noted no complications (0%) regarding GBR for vertical and horizontal bone augmentation, which is in disagreement with previous reports.[65,66] This might be further attributed to the complete edentulism of the subjects undergoing GBR which is easier to achieve primary wound closure due to no proximity of the nature dentition and any potential contamination associated with teeth. Moreover, in the authors' experience, wound dehiscence and membrane exposure typically occurs in the proximity of the dental structures. Last but not the least, it is important to note that in GBR for extensive atrophies, since no block harvesting surgery has to be performed, the patient is less likely subjected to complications regarding the donor site. Therefore, in the present report the high long-term survival rate and minimal peri-implant bone changes might be attributed to the lack of wound dehiscence due to adequate and smooth soft tissue management in combination to suitable biomaterial selection (i.e., type of membrane and bone graft). Therefore, our outcomes reported in this case series are in agreement with previous findings for horizontal[18–20,67] and vertical[22–27,47] bone augmentation utilizing similar bone graft mixture and membrane types.

In summary, these long-term results indicate that complete maxillary reconstruction can be achieved by means of GBR and maxillary sinus augmentation with a bone graft mixture of ABBM and AB and with the use of resorbable and non-resorbable barrier membranes with limited/no complications. It is very important to highlight that these procedures do require a significant clinical expertise in order to avoid surgical complications and to obtain successful results. Therefore, caution must be used to interpret these results. However, it is important to stress the

benefits of this approach over other treatments (i.e., block grafting): no complications at the donor site, no need for hospitalization, shortened treatment period, and less postoperative discomfort. Further, controlled trials must be conducted to investigate the effect of biomaterials as well as different approaches for extensive bone gain in the severely atrophied maxillary ridges.

CONCLUSION

Complete atrophied maxillary reconstruction can be successfully achieved by means of guided bone regeneration for horizontal and/or vertical bone gain including bilateral sinus augmentation when a mixture of anorganic bovine bone and autologous bone were used. Peri-implant bone level in the completely reconstructed maxilla showed minimal changes. Furthermore, proper training in hard and soft tissue management to avoid potential complications is imperative to achieve successful outcomes.

ACKNOWLEDGMENT

This paper was partially supported by the University of Michigan Periodontal Graduate Student Research Fund.

REFERENCES

1. Pietrokovski J, Massler M. Ridge remodeling after tooth extraction in rats. J Dent Res 1967; 46:222–231.
2. Pietrokovski J, Massler M. Alveolar ridge resorption following tooth extraction. J Prosthet Dent 1967; 17:21–27.
3. Cawood JI, Howell RA. A classification of the edentulous jaws. Int J Oral Maxillofac Surg 1988; 17:232–236.
4. Monje A, Monje F, Hernandez-Alfaro F, Gonzalez-Garcia R, Suarez-Lopez del Amo F, Galindo-Moreno P, Montanero-Fernandez J, Wang HL. Horizontal bone augmentation using autogenous block grafts and particulate xenograft in the severe atrophic maxillary anterior ridges: a cone-beam computerized tomography case series. J Oral Implantol 2015; 41(Spec No):366–371.
5. Schwarz F, Ferrari D, Balic E, Buser D, Becker J, Sager M. Lateral ridge augmentation using equine- and bovine-derived cancellous bone blocks: a feasibility study in dogs. Clin Oral Implants Res 2010; 21:904–912.
6. von Arx T, Buser D. Horizontal ridge augmentation using autogenous block grafts and the guided bone regeneration technique with collagen membranes: a clinical study with 42 patients. Clin Oral Implants Res 2006; 17:359–366.
7. Chiapasco M, Abati S, Romeo E, Vogel G. Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges. Clin Oral Implants Res 1999; 10:278–288.
8. Chiapasco M, Di Martino G, Anello T, Zaniboni M, Romeo E. Fresh frozen versus autogenous iliac bone for the rehabilitation of the extremely atrophic maxilla with onlay grafts and endosseous implants: preliminary results of a prospective comparative study. Clin Implant Dent Relat Res 2015; 17 (Suppl 1): e251–e266.
9. Monje A, Pikos MA, Chan HL, Suarez F, Gargallo-Albiol J, Hernandez-Alfaro F, Galindo-Moreno P, Wang HL. On the feasibility of utilizing allogeneic bone blocks for atrophic maxillary augmentation. Biomed Res Int 2014; 2014:814578.
10. Monje A, Chan HL, Suarez F, Galindo-Moreno P, Wang HL. Marginal bone loss around tilted implants in comparison to straight implants: a meta-analysis. Int J Oral Maxillofac Implants 2012; 27:1576–1583.
11. Monje A, Chan HL, Fu JH, Suarez F, Galindo-Moreno P, Wang HL. Are short dental implants (<10 mm) effective?. a meta-analysis on prospective clinical trials. J Periodontol 2013; 84:895–904.
12. Thoma DS, Zeltner M, Husler J, Hammerle CH, Jung RE. EAO Supplement Working Group 4 - EAO CC 2015 Short implants versus sinus lifting with longer implants to restore the posterior maxilla: a systematic review. Clin Oral Implants Res 2015; 26(Suppl):154–156.
13. Nkenke E, Stelzle F. Clinical outcomes of sinus floor augmentation for implant placement using autogenous bone or bone substitutes: a systematic review. Clin Oral Implants Res 2009; 20(Suppl 4):124–133.
14. Wallace SS, Froum SJ. Effect of maxillary sinus augmentation on the survival of endosseous dental implants. A systematic review. Ann Periodontol 2003; 8:328–343.
15. Aghaloo TL, Moy PK. Which hard tissue augmentation techniques are the most successful in furnishing bony support for implant placement? Int J Oral Maxillofac Implants 2007; 22(Suppl):49–70.
16. Urban IA, Lozada JL. A prospective study of implants placed in augmented sinuses with minimal and moderate residual crestal bone: results after 1 to 5 years. Int J Oral Maxillofac Implants 2010; 25:1203–1212.
17. Melcher AH. On the repair potential of periodontal tissues. J Periodontol 1976; 47:256–260.
18. Urban IA, Nagursky H, Lozada JL. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: a prospective case series in 22 patients. Int J Oral Maxillofac Implants 2011; 26:404–414.
19. Urban IA, Lozada JL, Jovanovic SA, Nagy K. Horizontal guided bone regeneration in the posterior maxilla using recombinant human platelet-derived growth factor: a case report. Int J Periodontics Restorative Dent 2013; 33: 421–425.

20. Urban IA, Nagursky H, Lozada JL, Nagy K. Horizontal ridge augmentation with a collagen membrane and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: a prospective case series in 25 patients. Int J Periodontics Restorative Dent 2013; 33:299–307.
21. Canullo L, Trisi P, Simion M. Vertical ridge augmentation around implants using e-PTFE titanium-reinforced membrane and deproteinized bovine bone mineral (bio-oss): a case report. Int J Periodontics Restorative Dent 2006; 26:355–361.
22. Simion M, Fontana F, Rasperini G, Maiorana C. Long-term evaluation of osseointegrated implants placed in sites augmented with sinus floor elevation associated with vertical ridge augmentation: a retrospective study of 38 consecutive implants with 1- to 7-year follow-up. Int J Periodontics Restorative Dent 2004; 24:208–221.
23. Simion M, Jovanovic SA, Trisi P, Scarano A, Piattelli A. Vertical ridge augmentation around dental implants using a membrane technique and autogenous bone or allografts in humans. Int J Periodontics Restorative Dent 1998; 18:8–23.
24. Urban I, Caplanis N, Lozada JL. Simultaneous vertical guided bone regeneration and guided tissue regeneration in the posterior maxilla using recombinant human platelet-derived growth factor: a case report. J Oral Implantol 2009; 35:251–256.
25. Urban IA, Jovanovic SA, Lozada JL. Vertical ridge augmentation using guided bone regeneration (GBR) in three clinical scenarios prior to implant placement: a retrospective study of 35 patients 12 to 72 months after loading. Int J Oral Maxillofac Implants 2009; 24:502–510.
26. Urban IA, Lozada JL, Jovanovic SA, Nagursky H, Nagy K. Vertical ridge augmentation with titanium-reinforced, dense-PTFE membranes and a combination of particulated autogenous bone and anorganic bovine bone-derived mineral: a prospective case series in 19 patients. Int J Oral Maxillofac Implants 2014; 29:185–193.
27. Urban IA, Monje A, Wang HL. Vertical ridge augmentation and soft tissue reconstruction of the anterior atrophic maxillae: a case series. Int J Periodontics Restorative Dent 2015; 35:613–623.
28. Wang HL, Boyapati L. "PASS" principles for predictable bone regeneration. Implant Dent 2006; 15:8–17.
29. Hammerle CH, Jung RE. Bone augmentation by means of barrier membranes. Periodontol 2000 2003; 33:36–53.
30. Hammerle CH, Jung RE, Feloutzis A. A systematic review of the survival of implants in bone sites augmented with barrier membranes (guided bone regeneration) in partially edentulous patients. J Clin Periodontol 2002; 29(Suppl 3):226–231; discussion 232–223.
31. Schlegel KA, Fichtner G, Schultze-Mosgau S, Wiltfang J. Histologic findings in sinus augmentation with autogenous bone chips versus a bovine bone substitute. Int J Oral Maxillofac Implants 2003; 18:53–58.
32. Scarano A, Degidi M, Iezzi G, Pecora G, Piattelli M, Orsini G, Caputi S, Perrotti V, Mangano C, Piattelli A. Maxillary sinus augmentation with different biomaterials: a comparative histologic and histomorphometric study in man. Implant Dent 2006; 15:197–207.
33. Galindo-Moreno P, Avila G, Fernandez-Barbero JE, Mesa F, O'Valle-Ravassa F, Wang HL. Clinical and histologic comparison of two different composite grafts for sinus augmentation: a pilot clinical trial. Clin Oral Implants Res 2008; 19:755–759.
34. Galindo-Moreno P, Hernandez-Cortes P, Mesa F, Carranza N, Juodzbalys G, Aguilar M, O'Valle F. Slow resorption of anorganic bovine bone by osteoclasts in maxillary sinus augmentation. Clin Implant Dent Relat Res 2013; 15:858–866.
35. Mordenfeld A, Hallman M, Johansson CB, Albrektsson T. Histological and histomorphometrical analyses of biopsies harvested 11 years after maxillary sinus floor augmentation with deproteinized bovine and autogenous bone. Clin Oral Implants Res 2010; 21:961–970.
36. Zijderveld SA, Schulten EA, Aartman IH, ten Bruggenkate CM. Long-term changes in graft height after maxillary sinus floor elevation with different grafting materials: radiographic evaluation with a minimum follow-up of 4.5 years. Clin Oral Implants Res 2009; 20:691–700.
37. Kahnberg KE, Ekestubbe A, Grondahl K, Nilsson P, Hirsch JM. Sinus lifting procedure. I. One-stage surgery with bone transplant and implants. Clin Oral Implants Res 2001; 12:479–487.
38. Esposito M, Grusovin MG, Coulthard P, Worthington HV. The efficacy of various bone augmentation procedures for dental implants: a Cochrane systematic review of randomized controlled clinical trials. Int J Oral Maxillofac Implants 2006; 21:696–710.
39. Misch CE, Perel ML, Wang HL, Sammartino G, Galindo-Moreno P, Trisi P, Steigmann M, Rebaudi A, Palti A, Pikos MA, Schwartz-Arad D, Choukroun J, Gutierrez-Perez JL, Marenzi G, Valavanis DK. Implant success, survival, and failure: the International Congress of Oral Implantologists (ICOI) Pisa Consensus Conference. Implant Dent 2008; 17:5–15.
40. Albrektsson T, Donos N, Working G. Implant survival and complications. The Third EAO consensus conference 2012. Clin Oral Implants Res 2012; 23(Suppl 6):63–65.
41. Mayfield L, Skoglund A, Nobreus N, Attstrom R. Clinical and radiographic evaluation, following delivery of fixed reconstructions, at GBR treated titanium fixtures. Clin Oral Implants Res 1998; 9:292–302.
42. Zitzmann NU, Scharer P, Marinello CP. Long-term results of implants treated with guided bone regeneration: a 5-year prospective study. Int J Oral Maxillofac Implants 2001; 16:355–366.
43. Jung RE, Fenner N, Hammerle CH, Zitzmann NU. Long-term outcome of implants placed with guided bone

regeneration (GBR) using resorbable and non-resorbable membranes after 12-14 years. Clin Oral Implants Res 2013; 24:1065–1073.

44. Donos N, Mardas N, Chadha V. Clinical outcomes of implants following lateral bone augmentation: systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). J Clin Periodontol 2008; 35:173–202.
45. Galindo-Moreno P, Fernandez-Jimenez A, Avila-Ortiz G, Silvestre FJ, Hernandez-Cortes P, Wang HL. Marginal bone loss around implants placed in maxillary native bone or grafted sinuses: a retrospective cohort study. Clin Oral Implants Res 2014; 25:378–384.
46. Galindo-Moreno P, Fernandez-Jimenez A, O'Valle F, Silvestre FJ, Sanchez-Fernandez E, Monje A, Catena A. Marginal bone loss in implants placed in grafted maxillary sinus. Clin Implant Dent Relat Res 2015; 17:373–383.
47. Simion M, Jovanovic SA, Tinti C, Benfenati SP. Long-term evaluation of osseointegrated implants inserted at the time or after vertical ridge augmentation. A retrospective study on 123 implants with 1-5 year follow-up. Clin Oral Implants Res 2001; 12:35–45.
48. Abassi YA, Xi B, Zhang W, Ye P, Kirstein SL, Gaylord MR, Feinstein SC, Wang X, Xu X. Kinetic cell-based morphological screening: prediction of mechanism of compound action and off-target effects. Chem Biol 2009; 16:712–723.
49. Galindo-Moreno P, Hernandez-Cortes P, Aneiros-Fernandez J, Camara M, Mesa F, Wallace S, O'Valle F. Morphological evidences of Bio-Oss(R) colonization by CD44-positive cells. Clin Oral Implants Res 2014; 25:366–371.
50. Galindo-Moreno P, Moreno-Riestra I, Avila G, Padial-Molina M, Paya JA, Wang HL, O'Valle F. Effect of anorganic bovine bone to autogenous cortical bone ratio upon bone remodeling patterns following maxillary sinus augmentation. Clin Oral Implants Res 2011; 22:857–864.
51. Del Fabbro M, Bellini CM, Romeo D, Francetti L. Tilted implants for the rehabilitation of edentulous jaws: a systematic review. Clin Implant Dent Relat Res 2012; 14:612–621.
52. Malo P, Nobre Mde A, Lopes I. A new approach to rehabilitate the severely atrophic maxilla using extramaxillary anchored implants in immediate function: a pilot study. J Prosthet Dent 2008; 100:354–366.
53. Sharma A, Rahul GR. Zygomatic implants/fixture: a systematic review. J Oral Implantol 2013; 39:215–224.
54. Testori T, Del Fabbro M, Capelli M, Zuffetti F, Francetti L, Weinstein RL. Immediate occlusal loading and tilted implants for the rehabilitation of the atrophic edentulous maxilla: 1-year interim results of a multicenter prospective study. Clin Oral Implants Res 2008; 19:227–232.
55. Del Fabbro M, Bortolin M, Taschieri S, Weinstein RL. Effect of autologous growth factors in maxillary sinus augmentation: a systematic review. Clin Implant Dent Relat Res 2013; 15:205–216.
56. Duyck J, Van Oosterwyck H, Vander Sloten J, De Cooman M, Puers R, Naert I. Magnitude and distribution of occlusal forces on oral implants supporting fixed prostheses: an in vivo study. Clin Oral Implants Res 2000; 11:465–475.
57. Chan HL, Monje A, Suarez F, Benavides E, Wang HL. Palatonasal recess on medial wall of maxillary sinus and clinical implications for sinus augmentation via lateral window approach. J Periodontol 2013; 84:1087–1093.
58. Pjetursson BE, Tan WC, Zwahlen M, Lang NP. A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. J Clin Periodontol 2008; 35:216–240.
59. Rickert D, Vissink A, Slater JJ, Meijer HJ, Raghoebar GM. Comparison between conventional and piezoelectric surgical tools for maxillary sinus floor elevation. A randomized controlled clinical trial. Clin Implant Dent Relat Res 2013; 15:297–302.
60. Wallace SS, Mazor Z, Froum SJ, Cho SC, Tarnow DP. Schneiderian membrane perforation rate during sinus elevation using piezosurgery: clinical results of 100 consecutive cases. Int J Periodontics Restorative Dent 2007; 27: 413–419.
61. Urban IA, Nagursky H, Church C, Lozada JL. Incidence, diagnosis, and treatment of sinus graft infection after sinus floor elevation: a clinical study. Int J Oral Maxillofac Implants 2012; 27:449–457.
62. Simion M, Trisi P, Piattelli A. Vertical ridge augmentation using a membrane technique associated with osseointegrated implants. Int J Periodontics Restorative Dent 1994; 14:496–511.
63. Chiapasco M, Zaniboni M, Boisco M. Augmentation procedures for the rehabilitation of deficient edentulous ridges with oral implants. Clin Oral Implants Res 2006; 17(Suppl 2):136–159.
64. Machtei EE. The effect of membrane exposure on the outcome of regenerative procedures in humans: a meta-analysis. J Periodontol 2001; 72:512–516.
65. Rocchietta I, Fontana F, Simion M. Clinical outcomes of vertical bone augmentation to enable dental implant placement: a systematic review. J Clin Periodontol 2008; 35:203–215.
66. Milinkovic I, Cordaro L. Are there specific indications for the different alveolar bone augmentation procedures for implant placement?. A systematic review. Int J Oral Maxillofac Surg 2014; 43:606–625.
67. Garaicoa C, Suarez F, Fu JH, Chan HL, Monje A, Galindo-Moreno P, Wang HL. Using cone beam computed tomography angle for predicting the outcome of horizontal bone augmentation. Clin Implant Dent Relat Res 2015; 17:717–723.